

## REMARKS

### Status of the Claims.

Claims 1, 3-5, 7-19, and 22-32 are pending with entry of this amendment, claims 2, 6, 20, and 21 having been cancelled and no claims being added. Claims 1, 3, 4, 5, 7, 8, 9, 17, and 22-26 are amended herein. These amendments introduce no new matter. Support is replete throughout the specification (*e.g.*, at page 4, line 25, in the claims as originally filed, *etc.*).

### Objections to the claims.

Claim 24 was objected to because of the recitation of "is shown" instead of "is as shown". Claim 24 is corrected with entry of this amendment thereby obviating this objection.

### 35 U.S.C. §102.

#### a) Kaneko *et al.*

Claims 1, and 3-5 were rejected under 35 U.S.C. §102(b) as allegedly anticipated by Kaneko *et al.* (1995) *DNA Res.*, 2: 153-166. Applicants traverse.

The Examiner is respectfully reminded that in order to make a *prima facie* case of anticipation, **all limitations** of the claims must be found in the cited reference or "fully met by it".

*Kalman v Kimberly-Clark Corp.*, 218 USPQ 781, 789 (Fed. Cir. 1983).

In the instant case claim 1 is directed to:

1. A composition comprising:  
**an apophytochrome polypeptide consisting of between about 190 amino acids and about 400 amino acids**, which apophytochrome polypeptide comprises a lyase domain, wherein said apoprotein polypeptide is selected from the group consisting of a plant apophytochrome polypeptide, an algal apophytochrome polypeptide, and a cyanobacterial apophytochrome polypeptide; and  
a bilin. [emphasis added]

The presently claimed invention is predicated, in part, on the discovery that a full length apophytochrome polypeptide is not required to form a fluorescent adduct (*i.e.*, a phytofluor), but rather **a truncated** apophytochrome polypeptide comprising a lyase domain is sufficient. Accordingly claim

1 is drawn to a composition comprising "an apophytochrome polypeptide consisting of between about 190 amino acids and about 400 amino acids" and comprising a lysase domain.

Kaneko *et al.* fails to disclose an apophytochrome polypeptide consisting of between about 190 amino acids and 400 amino acids. To the contrary, as recognized by the Examiner, Kaneko *et al.* teach a 1276 amino acid polypeptide.

Kaneko *et al.* also fails to disclose the formation of an adduct with a bilin and certainly fails to disclose the use of an apophytochrome fragment (lyase domain) to form an adduct with a bilin.

Kaneko *et al.* thus, does not provide all the elements of the presently claimed invention. The Examiner has failed to make her *prima facie* case and the rejection of claims 1, and 3-5 under 35 U.S.C. §102(b) in light of Kaneko *et al.* should be withdrawn.

**b) Yeh *et al.***

Claims 1, 7, and 9-11 were rejected under 35 U.S.C. §102(b) as allegedly anticipated by Yeh *et al.* (1997) *Science*, 277: 1505-1508. Applicants traverse.

As explained above, the presently pending claims are drawn to compositions comprising "an apophytochrome polypeptide consisting of between about 190 amino acids and about 400 amino acids" and "a bilin".

Yeh *et al.* describes a phytochrome-like open reading frames (ORFs) in the cyanobacterium *Synechocystis* sp. PCC6803 genome (*see*, page 1501, col. 1). One of the oRFs, locus slr09473 encodes a 748-residue polypeptide named CPH1. CPH1 comprises a second ORF, locus slr0474, that encodes a 147-amino acid protein, named rcpl which is related to the CheY superfamily of bacterial response regulators and contains aspartate kinase receiver modules (*see*, page 1505, col. 2).

Of these proteins, it is the full-length CPH1 that is described as a functional phytochrome with the ability to catalyze its own chromophore attachment.

Yeh *et al.* simply offers no teaching of an apophytochrome polypeptide consisting of between about 190 amino acids and 400 amino acids. Yeh *et al.* thus, does not provide all the elements of the presently claimed invention. The Examiner has failed to make her *prima facie* case and the rejection of claims 1, 7, and 9-11 under 35 U.S.C. §102(b) in light of Yeh *et al.* should be withdrawn.

**35 U.S.C. §103(a).**

**a) Yeh et al. and Stryer et al.**

Claims 12-16 were rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Yeh et al. (*supra.*) in view of Stryer et al. (U.S. Patent 4,859,582) (Office action, paragraph 7). In addition, claims 17-19, 22-23, 25, and 27-32 were rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Stryer et al. (*supra.*) in view of Yeh et al. (Office Action, paragraph 8). Applicants traverse.

The Examiner is respectfully reminded that *prima facie* case of obviousness requires that the combination of the cited art, taken with general knowledge in the field, must provide all of the elements of the claimed invention. When a rejection depends on a combination of prior art references, there must be some **teaching, suggestion, or motivation to combine** the references. *In re Geiger*, 815 2 USPQ2d 1276, 1278 (Fed. Cir. 1987). Moreover, to support an obviousness rejection, the cited references must additionally **provide a reasonable expectation of success**. *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991), *citing In re Dow Chemical Co.*, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988).

In the instant case, the claims, as amended herein pertain to compositions comprising ". . . **an apophytochrome polypeptide consisting of between about 190 amino acids and about 400 amino acids**, which apophytochrome polypeptide comprises a lyase domain. . . ." and a bilin, and to uses of such a composition.

Yeh et al. offers no teaching or suggestion of such a composition. To the contrary, Yeh et al. teaches a **full-length** phytochrome CPH1. There is no teaching or suggestion of a **truncated** apophytochrome comprising a lyase domain as recited in the presently pending claim.

Moreover, the defects of Yeh et al. **are not** cured by the citation of Stryer et al. To the contrary, Stryer et al. actually leads one of skill away from the presently claimed invention.

Stryer et al. teaches and suggests the creation and use of fluorescent adducts comprising phycobiliproteins, not apophytochromes as recited in the presently pending claims:

Compositions are provided comprising **biliproteins, (the term "biliproteins" is equivalent to the term "phycobiliproteins")** conjugated to a member of a specific binding pair, said pair consisting of ligands and receptors. [emphasis added] (col. 2, lines 49-53).

The Examiner is reminded that the phycobiliproteins disclosed by Stryer *et al.* and the phytochromes of the present invention are both **structurally and functionally very different proteins** (the only similarity between the two proteins is that they both occur as biliproteins (apoproteins attached to a bilin). A number of differences are listed below in Table 1.

**Table 1.** Differences between phytochromes (this application) and phycobiliproteins (Stryer *et al.* patent).

Property	Phytochrome	Phycobiliprotein
Fluorescence	Phytochromes <b><i>are not</i></b> naturally fluorescent.	Phycobiliproteins <b><i>are naturally strongly fluorescent.</i></b>
Self-assembly	Apophytochrome <b><i>will self assemble</i></b> with bilin to produce fluorescent product.	Phycobiliprotein <b><i>will not self assemble.</i></b> Phycobiliproteins require bilin lyase enzymes for proper assembly.
Function	Phytochromes are photoreceptors that control plant growth and development in response to light.	Present in light harvesting (photosynthetic) apparatus in cyanobacteria, eukaryotic algae.
Structure	"Invariant" Arg <b><i>not required.</i></b> Glu conserved in phycobiliprotein <b><i>not required.</i></b>	The Arg and Glu are not conserved in known phytochromes.
Sequence similarity	No substantial sequence similarity.	

Stryer *et al.* thus fails to teach or suggest a composition comprising "... an apophytochrome polypeptide consisting of between about 190 amino acids and about 400 amino acids" and actually lead one of skill away from the use of apophytochromes in favor of phycobiliproteins. The combination of Stryer *et al.* and Yeh *et al.* thus fails to teach or suggest the presently claimed invention and the rejection on these grounds should be withdrawn.

**b) Yeh *et al.*, Stryer *et al.*, and Clack *et al.***

Claim 24 was rejected under 35 U.S.C. §103(a) as allegedly obvious in light of Stryer *et al.* (U.S. Patent 4,859,582) and Yeh *et al.*, further in view of Clack *et al.*. Stryer *et al.* was cited as allegedly teaching a method of detecting a biomolecule, Yeh *et al.* was cited as allegedly teaching an apoprotein linked to a fluorescent adduct, and Clack *et al.* was cited as allegedly teaching SEQ ID NO:9. Applicants traverse.

As explained above, Yeh *et al.* **fails** to teach or suggest a composition comprising an apophytochrome fragment "... consisting of between about 190 amino acids and about 400 amino acids". Stryer *et al.* fails to remedy this defect because it teaches the use of phycobiliproteins rather than apophytochromes as recited in the presently pending claim.

Finally, contrary to the Examiner's assertion, Clack *et al.* does not disclose a protein consisting of SEQ ID NO:9 as recited in claim 24. To the contrary, the amino acid sequences disclosed by Clack *et al.* are 1164 and 1112 amino acids in length (*see, e.g.*, Figures 3A and 3B). In contrast, the sequence recited in claim 24 is 196 amino acids in length. There simply is no teaching or suggestion in the combination of Yeh *et al.*, Stryer *et al.*, and Clack *et al.* that would lead one of skill in the art to a composition comprising the 197 amino acid apophytochrome recited in claim 24.

Accordingly the Examiner has failed to make her *prima facie* case and the rejection of claim 24 on these grounds should be withdrawn.

**c) Yeh *et al.*, Stryer *et al.*, and Keneko *et al.***

Claim 26 was rejected under 35 U.S.C. §103(a) as allegedly obvious in light of Stryer *et al.* (U.S. Patent 4,859,582) and Yeh *et al.*, further in view of Kaneko *et al.*. Stryer *et al.* was cited as allegedly teaching a method of detecting a biomolecule, Yeh *et al.* was cited as allegedly teaching an apoprotein linked to a fluorescent adduct, and Kaneko *et al.* was cited as allegedly teaching Cph2, also known as SEQ ID NO:2. Applicants traverse.

As explained above, Yeh *et al.* **fails** to teach or suggest a composition comprising an apophytochrome fragment "... consisting of between about 190 amino acids and about 400 amino acids". Stryer *et al.* fails to remedy this defect because it teaches the use of phycobiliproteins rather than apophytochromes as recited in the presently pending claim.

Finally, contrary to the Examiner's assertion, Keneko *et al.* does not disclose a 190 to about 400 amino acid protein from Cph2 as recited in claim 26. To the contrary, Keneko *et al.* simply discloses an ORF analysis of 1,003,450 bp spanning map positions 64% to 92% of the genome of *Synechocystis* sp. Strain PCC6803 (*see, e.g.* abstract).

There simply is no teaching or suggestion in the combination of Yeh *et al.*, Stryer *et al.*, and Keneko *et al.* that would lead one of skill in the art to a composition comprising the 190 to 400 amino acid apophytochrome recited in claim 26.

Accordingly the Examiner has failed to make her *prima facie* case and the rejection of claim 26 on these grounds should be withdrawn.

In view of the foregoing, Applicants believes all claims now pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested. Should the Examiner seek to maintain the rejections, Applicants request a telephone interview with the Examiner and the Examiner's supervisor.

If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (510) 769-3513.

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Respectfully submitted,



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